IN THE UNITED STATES PATENT & TRADEMARK OFFICE

Applicant:	Grabowski, et al.	: Paper No:	
Serial No.	10/776,797	: Group Art Unit:	1632
Filed:	February 11, 2004	: Examiner:	Shen, Wu Cheng Winston

For: **LIPID HYDROLYSIS THERAPY FOR ATHEROSCLEROSIS AND RELATED DISEASES**

Confirmation No. 4885

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. 1.131

Dear Sir:

Gregory Grabowski and Hong Du, the inventors in the above-identified patent application (hereinafter, the Inventors), declare as follows:

1. The Xiao patent application, U.S. 2004/0038365, became available to the public on February 26, 2004, and was filed on October 26, 2001 as a PCT application, PCT/EP01/12382.

2. The Kapeller-Libermann application, U.S. 2002/0193303, became available to the public on December 19, 2002. This application claims priority to US 60/264,167, filed January 25, 2001.

3. The Inventors, Grabowski and Du, filed the above-identified patent application, serial number 10/776,796, which is a divisional of USSN 09/775,517 on February 11, 2004. Application 10/776,796 claims priority to US 6,849,257, filed February 2, 2001, and provisional application 60/180,363, filed February 4, 2000.

4. Prior to January 25, 2001, the Inventors conceived of and reduced the claimed invention to practice.

5. Prior to January 25, 2001, the Inventors conceived of a method of providing a biologically active lipid hydrolyzing protein to cells by administering a DNA sequence for a lipid hydrolyzing protein using a viral vector.

6. Prior to January 25, 2001, the Inventors reduced to practice a method for providing a biologically active lipid hydrolyzing protein to cells by administering a DNA sequence for a lipid hydrolyzing protein using a viral vector.

7. Prior to January 25, 2001, the Inventors reduced to practice the claimed invention as evidenced by the attached Exhibit A showing measurements of a biologically active lipid hydrolyzing protein (specifically, lysosomal acid lipase) activity. Activity was determined after administration of a viral vector, containing the DNA sequence for the protein, in mice deficient in LAL (LAL -/-) via a tail vein. The attached pages are unaltered from their original form except that all dates have been masked. (§1.131 Declaration - Exhibits A, B, C, D).

8. Exhibits A and C show raw data from mice obtained prior to January 25, 2001, wherein the mice had been injected with a vector comprising LAL DNA. Exhibits B and D show calculations of enzyme activity derived from this raw data, corresponding to Exhibits A and C, respectively. Collectively, these data show conception and reduction to practice of the claimed invention prior to January 25, 2001.

9. The Inventors state that all statements made herein of actual knowledge are true, or if made on information and belief are believed to be true.

10. The Inventors further state that all statements made herein were made with knowledge that willful false statements and the like are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that any such willful false statements may jeopardize the validity of this application or any patent issuing thereon.

Gregory Grabowski Date: 7/13/07

Hong Du Date: 7/27/07

CINLibrary 0010872.0522506 1745399v1

EXHIBIT A

LAL enzyme Assay						
Ad. Virus						
Sample #	**Genotype**	**Virus**	**Gain10**	**Gain5**	**Conversion (nmole/hr/mg)**	**U/mg**
1	+/+	II	618	314	8.147165	1.358E-04
1			623	319		
2	+/+	PBS	233	118	3.170895	5.285E-05
2			250	128		
3	+/+	I	297	151	4.050605	6.751E-05
3			320	165		
4	+/+	II	448	226	5.836285	9.727E-05
4			441	223		
5	-/-	PBS	156	77	2.11393	3.523E-05
5			166	86		
6	-/-	II	355	174	4.707105	7.845E-05
6			362	177		
7	-/-	I	192	98	2.63913	4.399E-05
7			210	102		
8	-/-	II	229	108	2.84921	4.749E-05
8			205	99		
9	-/-	PBS	189	95	2.409355	4.016E-05
9			178	86		
10	-/-	PBS	207	102	2.78356	4.639E-05
10			217	105		
11	-/-	I	1170	565	14.90255	2.484E-04
11			1100	545		
12	-/-	II	721	352	9.591465	1.599E-04
12			740	367		
14	-/-	I	282	137	4.050605	6.751E-05
14			335	164		
15	-/-	II	315	152	4.3329	7.222E-05
15			345	170		
Prep# 8256-167						
25			15	8	2215.6875	0.0369281
25			12	7		
5			52	26	1674.075	0.0279013
5			50	25		
Original			160	80	988.0325	0.0164672
Original			141	70		

A copy from Jill Bronnock's note book #1

H.DU

96

EXHIBIT B

LAL enzyme assay

100mg each sample liver

500µl lysis buffer

tube			
1	60H #5		
2	~~60J #12~~		
3	~~60J #10~~ 60J #9		
4	60J #10	345 NaAc	
5	40A1 #4	50 Substrate	
6	40A1 #1	5 Sample	
7	60H #6		
8	60H #8		
9	60J #12	(Gain Reading) X DF X .006565 X ~~#~~ X ~~time~~ 2	
10	80A6 #15	= nmole/hr/mg	
11	80A6 #14		
12	60J #11		
13	60H #7		
14	40A1 #3		
~~15~~			

	Gain 10	Gain 5				
			Blank	0	0	
#1	618/~~623~~	314/319	Blank	2	0	
#2	233/250	118/128				
#3	297/320	151/165	#8256-167	1:5²	15	8
#4	448/441	226/223		1:5²	12	7
#5	156/166	77/89		1:5¹	52	26
#6	355/362	174/177		1:5¹	50	25
#7	192/210	98/102		Orig	160	80
#8	229/205	108/99		Orig	141	70
#9	189/178	95/86				
#10	207/217	102/105				
* #11	1170/1100	565/545				
* #12	~~#~~721/740	352/367				
#14	282/335	137/164				
#15	315/345	~~345/345~~ 157/170				

EXHIBIT C

LAL Enzyme Assay							
Ad. Virus liver samples							
Genotype	Virus	Dilution Factor	Gain10	Gain5	Conversion (nmole/hr/mg)	U/mg	ug/ul
		Blank	0	0			
		Blank	3	2			
+/+	II	#1					1.3211
		125	93	45	160.8425	2.68E-03	
		125	103	51			
		25	438	210	165.438	2.76E-03	
		25	570	258			
		5	*	593	61.0545	1.02E-03	
		5	*	337			
+/+	PBS	#2					1.4348
		25	94	50	31.84025	5.31E-04	
		25	100	49			
		5	136	67	8.4032	1.40E-04	
		5	120	57			
+/+	I	#3					1.3247
		25	125	61	14.935375	2.49E-04	
		25	91	45			
		5	215	105	13.031525	2.17E-04	
		5	182	92			
+/+	II	#4					1.2787
		125	54	29	97.654375	1.63E-03	
		125	65	35			
		25	161	82	57.936125	9.66E-04	
		25	192	97			
		5	331	155	21.1393	3.52E-04	
		5	311	146			
-/-	PBS	#5					1.7653
		25	31	16	12.80175	2.13E-04	
		25	47	20			
		5	90	43	5.9085	9.85E-05	
		5	90	40			
-/-	II	#6					2.0912
		125	70	35	99.295625	1.65E-03	
		125	51	27			
		25	125	58	45.134375	7.52E-04	
		25	150	73			
		5	*247	120	22.78055	3.80E-04	
		5	347	167			

H copy from Jill Divinsky's

EXHIBIT D note book #1

H.DH

LAL Enzyme Assay — Ad Virus Livers (46) 20 [redacted] µl PBS + 5µl Sample

#1	1:5³	93	45	#5	1:5²	31	16
	1:5³	103	51		1:5²	47	20
	1:5²	438	210		1:5¹	90	43
	1:5²	570	258		1:5¹	90	40
†	1:5¹		593				
*	1:5¹		337				
				#6	1:5³	70	35
					1:5³	51	27
#2	1:5²	94	50		1:5²	125	58
	1:5²	100	49		1:5²	150	73
	1:5¹	136	67	*	1:5¹	247	120
	1:5¹	120	57		1:5¹	347	167
#3	1:5²	125	61	#7	1:5²	47	22
	1:5²	91	45		1:5²	55	25
	1:5¹	215	105		1:5¹	113	56
	1:5¹	182	92		1:5¹	110	52
#4	1:5³	54	29	#8	1:5²	60	31
	1:5³	65	35		1:5²	59	28
	1:5²	161	82		1:5¹	125	58
	1:5²	192	97		1:5¹	145	67
	1:5¹	331	195				
	1:5¹	311	146				
				# 8257-167	1:5²	70	32
Blank	0	0			1:5²	64	33
Blank	3	2			1:5¹	187	90
					1:5¹	—	—
					1:5⁰	650	320
* Suspect readings	Something wrong w/ substrate are too high				* 1:5⁰	790	384